Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Previously presented) A method of diagnosing the presence or severity of liver fibrosis in an individual, comprising the steps of:

(a) detecting α2-macroglobulin (α2-MG) in a sample from said individual;

(b) detecting hyaluronic acid (HA) in a sample from said individual;

(c) detecting tissue inhibitor of metalloproteinases-1 (TIMP-1) in a sample from said individual; and

(d) diagnosing the presence or severity of liver fibrosis in said individual based on the presence or level of α2-MG, HA and TIMP-1.

2. (Original) The method of claim **1**, comprising detecting at most three markers of fibrosis.

3. (Original) The method of claim **1**, further comprising detecting in a sample from said individual at least one marker selected from the group consisting of: PIIINP, laminin, tenascin, collagen type IV, collagen type VI, YKL-40, MMP-3, MMP-2, MMP-9/TIMP-1 complex, sFas ligand, TGF-β1, IL-10, apoA1, apoA2, and apoB.

4. (Original) The method of claim **3**, wherein said marker is YKL-40.

5. (Previously presented) The method of claim **1**, further comprising detecting in a sample from said individual two or more markers selected from the group consisting of PIIINP, laminin, tenascin, collagen type IV, collagen type VI, YKL-40, MMP-3, MMP-2, MMP-9/TIMP-1 complex, sFas ligand, TGF-β1, IL-10, apoA1, apoA2 and apoB.

6. (Original) The method of claim **1**, wherein said individual has viral hepatitis.

7. (Previously presented) The method of claim **6**, wherein said individual is infected with hepatitis C virus.

8. (Previously presented) The method of claim **6**, wherein said individual is infected with hepatitis B virus.

9. (Original) The method of claim **1**, wherein said individual has autoimmune liver disease.

10. (Original) The method of claim **1**, wherein said individual has alcoholic liver disease.

11. (Original) The method of claim **1**, wherein said individual has a fatty liver disease.

12. (Original) The method of claim **1**, wherein said individual has drug-induced liver disease.

13. (Original) The method of claim **1**, wherein step (a) comprises determining the level of α2-MG protein in said sample.

14. (Canceled)

15. (Previously presented) The method of claim **13**, wherein the level of α2-MG protein is determined using one or more anti-α2-MG antibodies.

16. (Original) The method of claim **1**, wherein step (a) comprises determining a level of α2-MG activity.

17. (Original) The method of claim **1**, wherein step (b) comprises determining the level of HA in said sample.

18. (Canceled)

19. (Previously presented) The method of claim **17**, wherein the level of HA is determined using one or more HA-binding proteins.

20. (Previously presented) The method of claim **17**, wherein the level of HA is determined using one or more anti-HA antibodies.

21. (Original) The method of claim **1**, wherein step (c) comprises determining the level of TIMP-1 protein in said sample.

22. (Canceled)

23. (Previously presented) The method of claim **21**, wherein the level of TIMP-1 protein is determined using one or more anti-TIMP-1 antibodies.

24. (Original) The method of claim **1**, wherein step (c) comprises determining a level of TIMP-1 activity.

25. (Original) The method of claim **1**,
wherein step (a) comprises determining the level of α2-MG protein,
wherein step (b) comprises determining the level of HA, and
wherein step (c) comprises determining the level of TIMP-1 protein.

26. (Original) The method of claim **25**, wherein the level of α2-MG protein, HA and TIMP-1 protein each is determined using an enzyme-linked assay.

27. (Original) The method of claim **1**, wherein a single sample is obtained from said individual.

28. (Original) The method of claim **27**, wherein said sample is selected from the group consisting of blood, serum, plasma, urine, saliva and liver tissue.

29. (Original) The method of claim **28**, wherein said sample is a serum sample.

30. (Previously presented) The method of claim **1**, comprising differentiating F0-F1 fibrosis from F2-F4 fibrosis.

31. (Previously presented) A method of differentiating F0-F1 fibrosis from F2-F4 fibrosis in an individual, comprising the steps of:

(a) contacting an appropriate dilution of a sample from said individual with anti-α2-MG antibody under conditions suitable to form a first complex of α2-MG and anti-α2-MG antibody;

(b) washing said first complex to remove unbound molecules;

(c) determining the amount of α2-MG-containing first complex;

(d) contacting an appropriate dilution of a sample from said individual with a HA-binding protein (HABP) under conditions suitable to form a second complex of HA and HABP;

(e) washing said second complex to remove unbound molecules;

(f) determining the amount of HA-containing second complex;

(g) contacting an appropriate dilution of a sample from said individual with anti-TIMP-1 antibody under conditions suitable to form a third complex of TIMP-1 and anti-TIMP-1 antibody;

(h) washing said third complex to remove unbound molecules;

(i) determining the amount of TIMP-1-containing third complex; and

(j) differentiating F0-F1 fibrosis from F2-F4 fibrosis in said individual based on the amounts of α2-MG, HA and TIMP-1-containing complexes.

32. (Previously presented) A method of monitoring the efficacy of anti-fibrotic therapy in a patient, comprising the steps of:

(a) detecting α2-macroglobulin (α2-MG) in a sample from a patient administered an anti-fibrotic therapy;

(b) detecting hyaluronic acid (HA) in a sample from said patient;

(c) detecting tissue inhibitor of metalloproteinases-1 (TIMP-1) in a sample from said patient; and

(d) determining the presence or severity of liver fibrosis in said patient based on the presence or level of α2-MG, HA and TIMP-1, thereby monitoring the efficacy of anti-fibrotic therapy.

33. (Original) The method of claim **32**, further comprising comparing the presence or severity of liver fibrosis determined in step (d) to the presence or severity of liver fibrosis in said patient at an earlier time.

34. (Original) The method of claim **32**, comprising detecting at most three markers of fibrosis.

35. (Original) The method of claim **32**, further comprising detecting in a sample from said patient at least one marker selected from the group consisting of: PIIINP, laminin, tenascin, collagen type IV, collagen type VI, YKL-40, MMP-3, MMP-2, MMP-9/TIMP-1 complex, sFas ligand, TGF-β1, IL-10, apoA1, apoA2, and apoB.

36. (Original) The method of claim **32**, wherein step (a) comprises determining the level of α2-MG protein in said sample.

37. (Original) The method of claim **36**, wherein the level of .alpha.2-MG protein is determined using one or more anti-α2-MG antibodies.

38. (Original) The method of claim **32**, wherein step (b) comprises determining the level of HA in said sample.

39. (Original) The method of claim **38**, wherein the level of HA is determined using one or more HA-binding proteins.

40. (Original) The method of claim **32**, wherein step (c) comprises determining the level of TIMP-1 protein in said sample.

41. (Original) The method of claim **40**, wherein the level of TIMP-1 protein is determined using one or more anti-TIMP-1 antibodies.

42. (Previously presented) A method of differentiating F0-F1 fibrosis from F2-F4 fibrosis in an individual, comprising the steps of:

(a) determining an α2-MG level in a sample from said individual;

(b) determining a HA level in a sample from said individual;

(c) determining a TIMP-1 level in a sample from said individual; and

(d) diagnosing said individual as having F0-F1 fibrosis when said α2-MG level is below an α2-MG cut-off value X1, said HA level is below a HA cut-off value Y1 or said TIMP-1 level is below a TIMP-1 cut-off value Z1,

diagnosing said individual as having F2-F4 fibrosis when said α2-MG level is above an α2-MG cut-off value X2, said HA level is above a HA cut-off value Y2 and said TIMP-1 level is above a TIMP-1 cut-off value Z2,

and diagnosing said individual as having an indeterminate status when said α2-MG level is above X1, said HA level is above Y1, and said TIMP-1 level is above Z1 but said α2-MG level is below X2, said HA level is below Y2 or said TIMP-1 level is below Z2.

43. (Original) The method of claim **42**, wherein said individual has a disorder selected from the group consisting of viral hepatitis, autoimmune liver disease, alcoholic liver disease, fatty liver disease and drug-induced liver disease.

44. (Original) The method of claim **43**, wherein said individual is infected with hepatitis C virus.

45. (Original) The method of claim **42**, wherein said samples are independently selected from the group consisting of blood, serum, plasma, urine, saliva and liver tissue.

46. (Previously presented) The method of claim **45**, wherein said α2-MG level, HA level and TIMP-1 level each is determined in a serum sample.

47. (Original) The method of claim **46**,
wherein X1 is a value between 1.8 and 2.2 mg/ml;
wherein Y1 is a value between 31 and 39 ng/ml;
wherein Z1 is a value between 900 and 1100 ng/ml;
wherein X2 is a value between 1.8 and 2.2 mg/ml;
wherein Y2 is a value between 54 and 66 ng/ml; and
wherein Z2 is a value between 1415 and 1735 ng/ml.

48. (Original) The method of claim **47**,
wherein X1=2.0 mg/ml;
wherein Y1=35 ng/ml;
wherein Z1 =1000 ng/ml;
wherein X2=2.0 mg/ml;
wherein Y2=60 ng/ml; and
wherein Z2=1575 ng/ml.

49. (Original) The method of claim **47**,
wherein X1=2.0 mg/ml;
wherein Y1=37 ng/ml;
wherein Z1=1100 ng/ml;
wherein X2=2.0 mg/ml;
wherein Y2=60 ng/ml; and

wherein Z2=1575 ng/ml.

50. (Previously presented) The method of claim **42**, wherein in a population having up to 30% liver fibrosis prevalence, X1, Y1, Z1, X2, Y2, and Z2 are independently selected to differentiate F0-F1 fibrosis from F2-F4 fibrosis in said individual with at least about 80% accuracy in at least 65% of the population assayed.

51. (Previously presented) The method of claim **42**, wherein in a population having up to 30% liver fibrosis prevalence, X1, Y1, Z1, X2, Y2, and Z2 are independently selected to differentiate F0-F1 fibrosis from F2-F4 fibrosis in said individual with at least about 90% accuracy in at least 65% of the population assayed.

52. (Currently amended) The method of claim **42**, wherein in a population having up to 30% liver fibrosis prevalence, X1, Y1, Z1, X2, Y2, and Z2 are independently selected to differentiate F0-F1 fibrosis from F2-F4 fibrosis in said individual with ~~achieve~~ a positive predictive value of at least 90% or a negative predictive value of at least 90% ~~for differentiating F0-F1 fibrosis from F2-F4 fibrosis~~ in at least 65% of the population assayed.

53. (Previously presented) The method of claim **42**, wherein in a population having up to 10% liver fibrosis prevalence, X1, Y1, Z1, X2, Y2, and Z2 are independently selected to differentiate F0-F1 fibrosis from F2-F4 fibrosis in said individual with at least about 90% accuracy in at least 70% of the population assayed.

54. (Currently amended) A method of diagnosing the presence or severity of liver fibrosis in an individual, comprising the steps of:

(a) comparing a level of a first fibrotic marker α2-MG in said individual to a cut-off value X1 to determine whether said individual is positive for α2-MG;

(b) comparing a level of a second fibrotic marker HA in said individual to a cut-off value Y1 to determine whether said individual is positive for HA;

(c) comparing a level of a third fibrotic marker TIMP-1 in said individual to a cut-off value Z1 to determine whether said individual is positive for TIMP-1; and

[[(c)]] (d) diagnosing the presence or severity of liver fibrosis in said individual based on positivity or negativity for α2-MG, ~~**and**~~ HA, and TIMP-1,

wherein in a population having ~~**up to 60%**~~ about 40% liver fibrosis prevalence, X1, **[[and]]** Y1, and Z1 are independently selected**[[,]]** to diagnose the presence or severity of liver fibrosis in said individual with ~~**at least about 70%**~~ more than 91% accuracy in about 70% of the population assayed.

55. (Canceled)

56. (Canceled)

57. (Currently amended) The method of claim **[[55]]** **54**, wherein the levels of at least three fibrotic markers are compared.

58. (Currently amended) The method of claim **[[55]]** **54**, wherein the levels of three fibrotic markers are compared.

59. (Currently amended) The method of claim **[[55]]** **54**, wherein the levels of at least four fibrotic markers are compared.

60. (Currently amended) The method of claim **[[55]]** **54**, wherein the levels of at least five fibrotic markers are compared.

61. (Previously presented) The method of claim **54**, wherein said diagnosis differentiates F0-F1 fibrosis from F2-F4 fibrosis.

62. (Canceled)

63. (Canceled)

64. (Canceled)

65. (Previously presented) A method of diagnosing the presence or severity of liver fibrosis in an individual, comprising the steps of:

(a) comparing a level of a first fibrotic marker α2-MG in said individual to a cut-off value X1 to determine whether said individual is positive for α2-MG;

(b) comparing a level of a second fibrotic marker HA in said individual to a cut-off value Y1 to determine whether said individual is positive for HA;

(c) comparing a level of a third fibrotic marker TIMP-1 in said individual to a cut-off value Z1 to determine whether said individual is positive for TIMP-1; and

(d) diagnosing the presence or severity of liver fibrosis in said individual based on positivity or negativity for α2-MG, HA, and TIMP-1,

wherein said cut-off values X1, Y1, and Z1 are independently selected to achieve an optimized clinical parameter selected from the group consisting of sensitivity, specificity, negative predictive value, positive predictive value, and accuracy.

66. (Canceled)

67. (Canceled)

68. (Original) The method of claim **65**, wherein said cut-off values are optimized using design of experiments (DOE) analysis.

69. (Currently amended) The method of claim **[[66]] 65**, wherein the levels of at least three fibrotic markers are compared.

70. (Currently amended) The method of claim **[[66]] 65**, wherein the levels of three fibrotic markers are compared.

71. (Previously presented) The method of claim **65**, wherein said diagnosis differentiates F0-F1 fibrosis from F2-F4 fibrosis.

72. (Currently amended) A method of diagnosing the presence or severity of liver fibrosis in an individual, comprising the steps of:

(a) comparing a level of a first fibrotic marker α2-MG in said individual to **[[two]]** a cut-off ~~values~~ value X1 ~~and X2~~ to determine whether said individual is positive for α2-MG, wherein said individual is positive for α2-MG when said level of α2-MG is above X1 ~~and X2~~;

(b) comparing a level of a second fibrotic marker HA in said individual to **[[two]]** a cut-off ~~values~~ value Y1 ~~and Y2~~ to determine whether said individual is positive for HA, wherein said individual is positive for HA when said level of HA is above Y1 ~~and Y2~~;

(c) comparing a level of a third fibrotic marker TIMP-1 in said individual to **[[two]]** a cut-off ~~values~~ value Z1 ~~and Z2~~ to determine whether said individual is positive for TIMP-1, wherein said individual is positive for TIMP-1 when said level of TIMP-1 is above Z1, ~~and Z2; and~~

wherein said individual positive for α2-MG, HA, and TIMP-1 is further evaluated for positivity for α2-MG, HA, and TIMP-1 using a second set of cut-off values X2, Y2, and Z2 comprising:

(d) comparing the level of α2-MG in said individual to X2, wherein said individual is positive for α2-MG when said level of α2-MG is above X2;

(e) comparing the level of HA in said individual to Y2, wherein said individual is positive for HA when said level of HA is above Y2;

(f) comparing the level of TIMP-1 in said individual to Z2, wherein said individual is positive for TIMP-1 when said level of TIMP-1 is above Z2; and

(g) diagnosing the presence or severity of liver fibrosis in said individual based on positivity or negativity for α2-MG, HA, and TIMP-1, wherein said cut-off values X2, Y2, and Z2 are greater than or equal to X1, Y1, and Z1, respectively, and wherein said cut-off values X1, Y1, Z1, X2, Y2, and Z2 are independently selected to achieve an optimized clinical parameter selected from the group consisting of sensitivity, specificity, negative predictive value, positive predictive value, and accuracy.

73. (Canceled)

74. (Previously presented) The method of claim **72**, wherein said cut-off values are optimized using design of experiments (DOE) analysis.